

In the Claims

1 1.(original) A composition comprising a polynucleotide sequence, wherein the
2 polynucleotide sequence comprises an *AIPL1* sequence within the LCA4 region of
3 chromosome 17p13 and is selected from the group consisting of a wild-type AIPL1 sequence
4 and a mutant AIPL1 sequence.

1 2.(currently amended) The composition of claim 1, wherein the mutants are selected
2 from the group consisting of Ala336Δ2, Trp278X, Cys239Arg, M79T, L88X, V96I, T124I,
3 P376S, Q163X, A197P, IVS2-2, G262S, R302L, P351D12, Cys42X (TGT -> TGA),
4 Val33ins 8 bp (GTGATCTT SEQ ID NO. 82), Leu257del 9 bp (CTCCGGCAC SEQ ID NO.
5 83) and mixtures and combinations thereof.

1 3.(original) A protein comprising SEQ. ID. NOs. 72-78 and variants of the protein of SEQ.
2 ID. NO. 72, or a polypeptide expressed by a polynucleotide comprising a nucleotide sequence
3 selected from the group consisting of SEQ. ID NOs. 1-8 or mutants of SEQ. ID. NO. 1
4 selected from the group consisting of SEQ. ID Nos. 9-41.

1 4.(original) A purified polynucleotide sequence comprising a sequence selected from the
2 group consisting of SEQ ID NOs. 1-71.

1 5.(original) A retinal disease diagnostic library comprising anti-sense DNA sequences, each
2 sequence corresponding to a DNA sequence including a mutation of the AIPL1 gene selected
3 from the group consisting of SEQ. ID Nos. 9-41 and mixtures and combinations thereof.

1 6.(original) A primer comprising an AIPL1 sequence, wherein the AIPL1 sequence is
2 selected from the group consisting of a wild-type AIPL1 sequence and a mutant AIPL1
3 sequence, wherein the mutant-AIPL1 contributes to a retinal disease.

1 7.(original) The primer of claim 6, further comprising a polynucleotide sequence selected
2 from the group consisting of SEQ ID NOs. 42-47 and 60-71.

1 8.(original) A probe comprising an AIPL1 sequence, wherein the AIPL1 sequence is
2 selected from the group consisting of a wild-type AIPL1 sequence and a mutant AIPL1
3 sequence, wherein the mutant-AIPL1 contributes to a retinal disease.

1 9.(original) A method to determine if an animal has a retinal disease or has a propensity to
2 pass a retinal disease to offspring, comprising the steps of:

- 3 (a) extracting polynucleotide from a cell or sample;
- 4 (b) determining if the polynucleotide contains a mutation in an AIPL1 encoding
5 or regulating region; and
- 6 (c) correlating the presence of the mutation as an indication of a retinal disease or
7 a propensity to pass a retinal disease to offspring.

1 10.(original) The method of claim 9, further comprising the steps of:

- 2 obtaining a patient sample; and
- 3 amplifying the polynucleotide.

1 11.(original) The method of claim 10, wherein the amplifying is done via polymerase chain
2 reaction.

1 12.(original) The method of claim 9, wherein the determining is done via polynucleotide
2 sequence.

1 13.(currently amended) The method of claim 9, wherein the mutations are selected from
2 the group consisting of Ala336Δ2, Trp278X, Cys239Arg, M79T, L88X, V96I, T124I,
3 P376S, Q163X, A197P, IVS2-2, G262S, R302L, P351D12, Cys42X (TGT -> TGA),

4 Val33ins 8 bp (GTGATCTT SEQ ID NO. 82), Leu257del 9 bp (CTCCGGCAC SEQ ID NO.
5 83) and mixtures and combinations thereof.

1 14.(original) A therapeutic method to treat retinal disease comprising the step of
2 administering to an animal an effective amount of a protein encoded by a wild-type AIPL1
3 gene or a polynucleotide sequence a wild-type AIPL1 gene or a retinal medication designed
4 to ameliorate disease symptoms to the patient if the mutation is detected or mixtures or
5 combinations thereof.

1 15.(original) The method of claim 14, wherein the medication is an drug that inhibits retinal
2 cell death.

1 16.(currently amended) The method of claim 14, wherein the mutations are selected from
2 the group consisting of Ala336Δ2, Trp278X, Cys239Arg, M79T, L88X, V96I, T124I,
3 P376S, Q163X, A197P, IVS2-2, G262S, R302L, P351D12, Cys42X (TGT -> TGA),
4 Val33ins 8 bp (GTGATCTT SEQ ID NO. 82), Leu257del 9 bp (CTCCGGCAC SEQ ID NO.
5 83) and mixtures and combinations thereof.

1 17.(original) A method to determine if a patient has a mutant AIPL1 gene comprising:
2 (a) extracting AIPL1 polypeptide from a cell or sample from the patient;
3 (b) determining if the polypeptide contains an AIPL1 mutation; and
4 (c) correlating the mutation as an indication of a retinal disease.

1 18.(currently amended) The method of claim 17, wherein the mutations are selected from
2 the group consisting of Ala336Δ2, Trp278X, Cys239Arg, M79T, L88X, V96I, T124I,
3 P376S, Q163X, A197P, IVS2-2, G262S, R302L, P351D12, Cys42X (TGT -> TGA),
4 Val33ins 8 bp (GTGATCTT SEQ ID NO. 82), Leu257del 9 bp (CTCCGGCAC SEQ ID NO.
5 83) and mixtures and combinations thereof.

1 19.(original) A method of producing a cell expressing an AIPL1 mutation comprising
2 transfected a cell with a polynucleotide sequence having at least one AIPL1 mutation in the
3 sequence.

1 20.(currently amended) The method of claim 19, wherein the encoded mutation is
2 selected from the group consisting of are selected from the group consisting of Ala336Δ2,
3 Trp278X, Cys239Arg, M79T, L88X, V96I, T124I, P376S, Q163X, A197P, IVS2-2, G262S,
4 R302L, P351D12, Cys42X (TGT -> TGA), Val33ins 8 bp (GTGATCTT SEQ ID NO. 82),
5 Leu257del 9 bp (CTCCGGCAC SEQ ID NO. 83) and mixtures and combinations thereof.

1 21.(original) A method for determining the presence of an AIPL1 mutant in a patient
2 sample, which comprises:

- 3 (a) isolating polynucleotide extracted from the patient sample;
- 4 (b) hybridizing a detectably labeled oligonucleotide to the polynucleotide isolated
5 in step (b), the oligonucleotide having at its 3' end at least 15 nucleotides
6 complementary to a wild type polynucleotide sequence having at least one
7 mutation;
- 8 (c) attempting to extend the oligonucleotide at its 3'-end;
- 9 (d) ascertaining the presence or absence of a detectably labeled extended
10 oligonucleotide; and
- 11 (e) correlating the presence or absence of a detectably labeled extended
12 oligonucleotide in step (e) with the presence or absence of a AIPL1 mutation.

1 22.(original) The method of claim 21, further comprising taking a patient sample prior to the
2 isolating step.

1 23.(original) The method of claim 21, wherein the isolated nucleic acid is amplified prior

2 to hybridization.

1 24.(original) The method of claim 21, wherein the detectable label on the oligonucleotide
2 is an enzyme, radioisotope or fluorochrome.

1 25.(currently amended) A test kit useful for the detection of AIPL1 mutations comprising
2 a container containing at least one polynucleotide capable of hybridizing with a
3 polynucleotide encoding at least one mutation selected from the group consisting of
4 Ala336Δ2, Trp278X, Cys239Arg, M79T, L88X, V96I, T124I, P376S, Q163X, A197P, IVS2-
5 2, G262S, R302L, P351D12, Cys42X (TGT -> TGA), Val33ins 8 bp (GTGATCTT SEQ ID
6 NO. 82), Leu257del 9 bp (CTCCGGCAC SEQ ID NO. 83) and mixtures and combinations
7 thereof.

1 26.(currently amended) A method of screening compounds to determine their
2 effectiveness in counteracting a cell's retinal behavior due to a mutation in its AIPL1 gene
3 comprising:

4 (a) contacting the compound with a cell including a mutation in its AIPL1 gene
5 where the mutation is selected from the group consisting of Ala336Δ2,
6 Trp278X, Cys239Arg, M79T, L88X, V96I, T124I, P376S, Q163X, A197P,
7 IVS2-2, G262S, R302L, P351D12, Cys42X (TGT -> TGA), Val33ins 8 bp
8 (GTGATCTT SEQ ID NO. 82), Leu257del 9 bp (CTCCGGCAC SEQ ID NO.
9 83) and mixtures and combinations thereof; and

10 (b) determining if the cell is affected by the compound.

1 27.(original) A method to determine if a cell or sample has an AIPL1 mutation comprising:

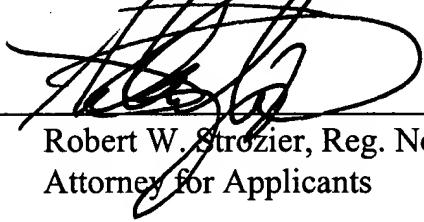
2 (a) extracting polynucleotide from a cell;
3 (b) amplifying polynucleotides which encode AIPL1; and
4 (c) determining if the polynucleotide contains a mutation;

5

- (d) correlating the presence of the mutation as an indication of a retinal disease or a propensity to pass a retinal disease to offspring.

If you have any question, please call.

Respectfully submitted,



Robert W. Strozier, Reg. No. 34,024
Attorney for Applicants

Date: July 5, 2005